Remarks/Arguments

Applicants respectfully request reconsideration of this application in view of the amendments set forth above and the remarks set forth below. Claims 1-97 are in the application. Claims 1-94 have been objected to, Claims 95-96 have been rejected, and Claim 97 has been allowed. Applicants amendments above cancel Claims 2, 6-9, 20, 24-27, 29-34, 40-43, 48-51, 53-66 and 68-94, leaving pending Claims 1, 3-5, 10-19, 21-23, 28, 35-39, 44-47, 52, 67 and 95-97.

Claims 1-94 have been objected to because they contain non-elected subject matter, which subject matter the Examiner has withdrawn from consideration. In response to this objection, Applicants have amended Claims 1 and 3-5 and canceled Claims 2, 6-9, 20, 24-27, 29-34, 40-43, 48-51, 53-66 and 68-94 to eliminate non-elected subject matter. Applicants reserve the right to file one or more divisional applications covering the canceled subject matter. In view of these amendments, Applicants believe that the objection should be removed and Claims 1, 3-5, 10-19, 21-23, 28, 35-39, 44-47, 52, and 67 should be allowed.

Claims 95 and 96 have been rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make or use the invention. Claims 95-96 have been amended merely to make more precise the reference to Claim 1, since Claim 1 covers a compound rather than a pharmaceutical composition. Applicants traverse this rejection for the reasons set forth below.

The purpose of the enablement requirement is to ensure that the invention is communicated to the interested public in a meaningful way. The enablement requirement is separate and distinct from the description requirement. MPEP 2164.

The standard for determining whether the enablement requirement is met is whether the experimentation needed to practice the invention is undue or unreasonable. Even experimentation which may be complex is not necessarily undue if the art typically engages in such experimentation. MPEP 2164.01.

The Examiner bears the burden for establishing a lack of enablement. A specification which teaches how to make and use the invention must be taken as complying with the enablement requirement unless there is reason to doubt the truth of the statements

in the specification. MPEP 2164.04. The Examiner has not asserted, nor provided any evidence to indicate, that any of the data or statements in the specification are incorrect or untrue.

Claim 95 is directed to a method of inhibiting the phospholipase activity of an enzyme in a mammalian subject in need thereof comprising administering to said subject a therapeutically effective amount of a compound of Claim 1. Claim 96 is directed to a method of treating an inflammatory response in a mammalian subject in need thereof comprising administering to said subject a therapeutically effective amount of a compound of Claim 1. The specification clearly teaches how to make and administer compounds of Claim 1 for the inhibition of phospholipase activity and treatment of inflammation, for example, on pages 159-180 of the specification.

The Examiner has stated that the specification does not enable one skilled in the art to use the invention commensurate in scope with this claim. Applicants deem the Examiner's statement wholly inconsistent with the experimental evidence and written description provided in the specification. The specification makes clear in the examples and elsewhere that the administration of the claimed compounds will inhibit phospholipase activity in a mammal. Once administered, it is reasonable to expect that this inhibition will be effective against any disease state that involves such activity. Those skilled in the pharmaceutical art routinely test compounds for activity in treating disease states, and any experimentation which may be needed to confirm efficacy in a particular case would not be undue or unreasonable to those skilled in the art.

In the specification, Applicants clearly describe in detail how to make and administer a formulation of any and all of the claimed compounds, and further teach that administration thereof will inhibit phospholipase activity and will be effective to treat inflammation and other disease states related to such activity. Specific information regarding making and using the invention is provided, for example, on page 163, lines 15-23. One skilled in that art would have absolutely no difficulty understanding how to make or administer the compounds or formulations described in the specification.

Applicants' specification provides a great deal of data showing inhibition of phospholipase activity by the claimed compounds, such as in the LysoPC assay in Example 86 and Table 1, found on pages 159-169 of the specification. Applicants' specification further provides a great deal of data showing that the presently claimed compounds inhibit

phospholipase activity and reduce inflammation in vivo in a mammal, particularly in rat paw edema tests described on page 163 and in Table 2, pages 170-172, of the specification.

On page 172 of the specification, Applicants state: "The compounds of this invention inhibit Cytosolic Phospholipase A2 (cPLA2) activity which is required for supplying arachidonic acid substrate to cyclooxygenase –1 or 2 and 5-lipoxygenase, which in turn initiates the production of prostaglandins and leukotrienes, respectively. In addition, cPLA2 activity is essential for producing the lyso-phospholipid precursor to Platelet Activating Factor (PAF). Thus, these compounds are useful in the treatment and prevention of disease states in which leukotrienes, prostaglandins or PAF are involved." A variety of disease states involving these entities are well-known to those skilled in the art.

The Examiner has stated that "the prior arts do not indicate that the instant compound is useful in treating all forms of diseases that relate to inhibition of phospholipase activity." The Examiner also has started that "the prior arts do not indicate that the instant compound is useful in treating all forms of inflammatory response." Although these statements may be true, such prior art is not required to establish enablement or patentability. Sufficient information is contained in the specification to provide an enabling disclosure without reference to the prior art.

Applicants agree with the Examiner's assertion that the level of skill in the art is high. Those skilled in the art will be readily able to test the efficacy of the invention for treating whatever inflammatory response is of interest to them without experimentation that would be unreasonable or undue for such skilled practitioners who are accustomed to performing such tests.

The Examiner has stated that "each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit [sic] from this activity". The Examiner has failed to state the source of this incredibly burdensome requirement; it is certainly not found in the patent laws of the United States. Applicants are not required to test every embodiment of the invention, nor to test the claimed compounds for use against every possible disease which they may treat. If the Examiner believes that there is such a requirement, Applicants respectfully request that the Examiner point out where in the patent law such a requirement is found.

The Examiner's apparent belief that a patent specification must include tests of every embodiment of the invention would make it almost impossible to claim a broad invention. However, Congress has legislated a patent system that allows inventors to claim their inventions more broadly than the scope of their experimental examples, and which system, in fact, does not require such examples. The Examiner is not empowered to remake this system.

As long as the specification discloses at least one method for making and using the claimed invention, the enablement requirement is satisfied. MPEP 2164.01(b).

The Examiner's reference to the Genentech case is inapposite: Applicants have successfully concluded a search for compounds and methods that are effective in inhibiting phospholipase activity and treating related disease states, such as inflammation, and have clearly described how to make and use the claimed invention. Applicants have further provided detailed experimental evidence to support their statements and claims. The claimed invention is not a vague intimation of a general idea that may or may not work, but is a real invention that is supported by evidence that it does work. Although not a requirement for patentability, this invention has actually been reduced to practice as shown by the tests in the specification.

Applicants disagree with the Examiner's view of the unpredictability of the results of using the claimed invention. Applicants have shown that the claimed compounds inhibit phospholipase activity, and it is quite reasonable to assume that the administration of these compounds according to the disclosure of the specification will be useful in treating diseases that involve phospholipase activity. Applicants have shown that the claimed compounds are useful for treating inflammation involving phospholipase activity.

Applicants have provided sufficient guidance in the specification to allow those skilled in the art to practice the invention. Applicants are not required by law to state the mechanism or action or specific treatment protocol for every form of disease related to phospholipase inhibition in order to meet the enablement requirement of 35 U.S.C. 112.

Applicants agree with the Examiner that the pharmaceutical arts involve in vitro and in vivo tests to determine which compounds exhibit the desired activity. The specification is evidence that Applicants have indeed conducted such tests, and as a result of these tests have identified the claimed compounds, compositions and methods. The Examiner is incorrect, however, in her stated belief that it is a requirement for patentability to test every

embodiment of the invention. Furthermore, because such testing is routine in the art, such testing does not constitute undue experimentation. In fact, anyone who wants to sell a claimed compound or composition for pharmaceutical use will need to do many tests to obtain approval from the relevant regulatory authorities. However, Applicants are not required to do such testing in order to obtain patent protection.

The Examiner has stated that there are no working examples of how the claimed compound is used to treat inflammatory response. Applicants respectfully disagree, and direct the Examiner's attention to Example 87 and Table 2. The Examiner also has indicated that the examples are insufficient to support a broad claim to inhibition of phospholipase activity. Applicants again respectfully disagree. The examples in the specification provide sufficient evidence of phospholipase inhibition and efficacy in treating inflammation in a mammal. Furthermore, working examples are not required for patentability in the United States.

The breadth of the Claims 95 and 96 is commensurate with the breadth of the disclosure. It is reasonable to expect that inflammation and other disease states involving phospholipase activity can be treated with a phospholipase inhibitor. Both phospholipase inhibition and inflammation reduction have been demonstrated in the specification examples. The specification has detailed numerous diseases that can be treated with the claimed inhibitors. Absolute proof that the claimed inhibitors are efficacious against every such disease or for every type of inflammatory response is not required by 35 U.S.C. 112, first paragraph.

The Examiner has stated that "numerous amount of modifications" would be needed to use the compound as claimed. This statement is not understood. What does the Examiner imagine would need to be modified? What evidence is there to support this assertion? The Examiner has not provided a proper explanation on this point and Applicants respectfully request clarification. Applicants believe that the specification has provided a clear, detailed description of how to make and use the invention with no need for numerous modifications.

The Examiner has suggested that Applicants can overcome the rejection of Claim 96 by limiting Claim 96 to a certain limited list of diseases, but has not explained why she believes that the specification is enabling with regard to the treatment of these diseases and not with regard to other diseases mentioned in the specification. The Examiner's implied

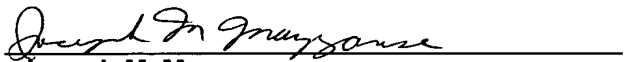
admission that the enablement requirement is met for these embodiments of Claim 96 suggests that the rejection of Claim 96 should not stand.

No undue experimentation would be required by those skilled in the art to make and use the claimed invention. The description, experimental examples, and data presented in the specification are sufficient to meet the legal standard for enablement of Claims 95 and 96.

For all the foregoing reasons, Applicants believe that the enablement requirement of 35 U.S.C. 112, first paragraph, has been met and respectfully request withdrawal of the instant rejections of Claims 95 and 96.

Applicants have amended the first paragraph of the specification to correct the continuing data, as suggested by the Examiner.

Applicants believe that Claims 1, 3-5, 10-19, 21-23, 28, 35-39, 44-47, 52, 67 and 95-97 are all in condition for allowance and advancement to issue and solicit such action at an early date.



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